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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/663,454 | 09/15/2003 | James D. Murray | UCAL-286 | 4027 |
| 24353 | 7590 | 12/15/2006 | EXAMINER | |
| BOZICEVIC, FIELD & FRANCIS LLP 1900 UNIVERSITY AVENUE SUITE 200 EAST PALO ALTO, CA 94303 | | | HAMA, JOANNE | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1632 | |

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|---------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/663,454 | Applicant(s) MURRAY ET AL. | |
| | Examiner Joanne Hama, Ph.D. | Art Unit 1632 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 September 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,13-15,20,21,33,35,36 and 38-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,13-15,20,21,33,35,36 and 38-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant filed a response to the Non-Final Action of March 28, 2006 on September 27, 2006. Claims 2, 4-12, 16-19, 22-32, 34, 37, 44-48 are cancelled. Claims 1 and 13 are amended.

Claims 1, 3, 13-15, 20, 21, 33, 35, 36, 38-43 are under consideration.

Withdrawn Rejections

35 U.S.C. § 112, 1st parag. Written Description

Applicant's arguments, see pages 5-10 of Applicant's response, filed September 27, 2006, with respect to the rejection of claims 1, 3, 5, 6, 13-15, 17-21, 33, 35, 36, 38-48 have been fully considered and are persuasive. Applicant has amended the claims from "fatty acid desaturase" to "stearoyl coenzyme A desaturase" (SCD) and that the SCD has the specific activity of "delta-9-desaturase activity." These amendments have been found persuasive. The rejection of claims 1, 3, 13-15, 20, 21, 33, 35, 36, 38-43 has been withdrawn. It is noted that the rejection of claims 5, 6, 17-19, 44-48 are withdrawn as the claims are cancelled.

Examiner's note: Based on the teachings of the art, there is support for the breadth of stearoyl coenzyme A desaturase (SCD) from any species of animal having delta-9 desaturase activity. In particular, Pereia et al., 2003, Prostaglandins, Leukotrienes, and Essential Fatty Acids, 68, 97-106, submitted by Applicant in Applicant's declaration, December 1, 2005, teach that stearoyl CoA (Δ 9) desaturase catalyzes the first step in the PUFA biosynthetic pathway, namely the incorporation of a

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double bond at carbon #9 of stearic acid to generate oleic acid. Pereira et al. teach that the SCD gene has been isolated from different species including mouse, human, fish, and insects. Pereira et al. teach that the presence of two long hydrophobic domains capable of spanning the lipid bilayer twice, and three conserved histidine-box motifs containing eight histidine residues with the general structure $HX_{(3-4)}H$, $HX_{(2-3)}HH$, $HX_{(2-3)}HH$. Each of these histidines residues is essential for the catalytic activity of this enzyme as demonstrated by site-directed mutagenesis (Pereira et al., page 99, 1st col. under "2.2.1 Stearoyl CoA ($\Delta 9$) desaturase (SCD)", see also Shanklin et al., 1994, Biochemistry, 33: 12787-12794, who carried out the mutagenesis study).

It is noted that while the art teaches that heterologous proteins are frequently found to have unexpected effects or no effect in transgenic animals that express them (e.g. Hammer et al., 1986, J. Anim. Sci., 63: 269-278), the Examiner does not have reason to believe that the instant invention has the issue of unexpected or no effect in the milk of the claimed transgenic non-human mammal because the substrate of SCD ($\Delta 9$) is a fatty acid and not a protein. Also note that Shanklin et al., teach that rat SCD ($\Delta 9$) complements a yeast strain deficient for $\Delta 9$ desaturase activity (Shanklin et al., abstract), thus illustrating that rat SCD has appropriate activity in a distantly related organism.

As such, the art appears to provide support for the claimed scope.

35 U.S.C. § 112, 1st parag.-Enablement

Applicant's arguments, see pages 10-13 of Applicant's response, filed September 27, 2006, with respect to the rejection of claims 1, 3, 5, 6, 13-15, 17-21, 33, 35, 36, 38-48 have been fully considered and are persuasive. The rejection of claims 1, 3, 13-15, 20, 21, 33, 35, 36, 38-43 has been withdrawn. It is noted that the rejection of claims 5, 6, 17-19, 44-48 are withdrawn as the claims are cancelled.

Applicant has amended the claims from "fatty acid desaturase" to "stearoyl coenzyme A desaturase" (SCD) and that the SCD has the specific activity of "delta-9-desaturase activity." In response, this amendment is found persuasive, see Examiner's note, above in the withdrawal of the Written Description rejection for further explanation. The rejection as it applies to this issue is withdrawn.

Regarding the issue of the non-human transgenic mammal encompassing mammals wherein the transgene is not stably integrated in the genome (e.g. plasmid), Applicant has amended the claim to indicate that the transgene is "chromosomally integrated." This amendment is found persuasive and the rejection as it applies to this issue is withdrawn.

Regarding the issue that the claims are drawn to cloning of any non-human mammal, the rejection is withdrawn as Applicant has cancelled the claims drawn to this issue (claims 18 and 46).

Regarding the issue that the claims result in a tetraploid mammal (claims 18 and 46, step b), the rejection is withdrawn as Applicant has cancelled the claims drawn to this issue.

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35 U.S.C. § 112, 2nd parag.

Applicant's arguments, see page 13 of Applicant's response, filed September 27, 2006, with respect to the rejection of claims 18 and 40 have been fully considered and are persuasive. Applicant indicates that claim 18 is cancelled and that the inclusion of claim 40 in the rejection appears to be inadvertent as claim 40 has no steps a-c. The rejection of claims 18 and 40 has been withdrawn.

Examiner's note 2, regarding state of the prior art and the instant application:

The claimed invention appears to be free of art. The closest arts are Ward et al, 1997, Biochemical Society Transactions, 25: S673, abstract No. 145, previously cited by Examiner (September 2, 2004) and Medran et al., 2000, Pflugers Archive European Journal of Physiology, 439: R24. Ward et al. teach that it would be advantageous to express SCD ($\Delta 9$) as a transgene in ruminant carcass, in order to arrive at carcass that has an increased proportion of monounsaturated fatty acids (MUFA). Medran et al. teach that genetic markers were used to identify natural DNA sequence variability in a variety of candidate genes that determine the fatty acid composition in milk. Medran et al. teach that an important selection objective is to increase the proportion of unsaturated fatty acids, to make a healthier product and softer more marketable butter. One particular gene candidate was SCD. While there is motivation to combine the teachings of the two references, an artisan cannot reasonably predict that expression of a transgene comprising the nucleic acid sequence encoding SCD would result in milk

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that is at least 5% higher in MUFA than in milk produced by a non-transgenic mammal of the same species.

New Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 13-15, 20, 21, 33, 35, 36, 38-43 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 3 recites the limitation "said fatty acid desaturase." There is insufficient antecedent basis for this limitation in the claim. It is unclear what the antecedent basis of "fatty acid desaturase" is. Claims 3, 13-15, 20, 21, 33, 35, 36, 38-43 depend on claim 1 and are thus included in the rejection.

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: 1) that the SCD has delta-9 desaturase activity, 2) that the embryo is transplanted into a pseudopregnant female and 3) that the claimed non-human mammal is identified, wherein identification is achieved by selecting the transgenic non-human mammal that has the transgene stably integrated in its genome and that the said transgenic non-human mammal produces milk comprising a level of monounsaturated fatty acids (MUFA) that is at least 5%

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higher than the level of MUFA in milk produced by a non-transgenic mammal of the same species. Claims 14, 15 depend on claim 13 and are thus included in the rejection.

A suggested amended claim 13 is as follows:

A method for producing a non-human transgenic mammal of claim 1, said method comprising:

a) introducing a transgene construct into a single-cell embryo wherein the transgene construct comprises a nucleotide sequence encoding steroyl-coenzyme A desaturase (SCD) having delta-9 desaturase activity, operably linked to a mammary gland-specific promoter,

b) transplanting said single-cell embryo into a recipient pseudopregnant female of the same species,

c) allowing said single-cell embryo to develop to term,

d) identifying a transgenic non-human mammal whose genome comprises the transgene construct, wherein said transgenic non-human mammal produces milk comprising a level of monounsaturated fatty acids (MUFA) that is at least 5% higher than the level of MUFA in milk produced by a non-transgenic mammal of the same species.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-

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272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

